

**REMARKS**

Entry of the foregoing and reconsideration of the above-identified application in view of the foregoing amendments and the following remarks, are respectfully requested.

Applicants would first like to thank Technology Center Director John Doll, Interference Specialist and SPE Michael Woodward, and Technology Center Practice Specialist George Elliott for the courtesy of granting the undersigned an interview to discuss this application. During the interview, Applicants' representatives discussed the position of Examiner Brusca regarding the definition of "stochastic" as used in the Kauffman specification and claims. It is believed that agreement was reached, based at least in part on the use of "stochastic" in the dependent claims (see in particular, Claim 17 of the Kauffman '323 patent) that "stochastic" must encompass random. As such, declaration of an interference with various Kauffman patents and Claims 29-48 is entirely appropriate.

Upon entry of the foregoing amendments, new Claims 29-48 will be pending in this application. New Claims 29-48 are identical to Claims 3, 4, 6-8 and 11-27 which are based on (1) Claims 3-14, originally presented on March 3, 1999, which were amended on June 9, 1999 with Applicants' original Request for Interference and on April 14, 2000 with Applicants' Renewed Request for Interference, (2) Claims 15-25 added on June 9, 1999 and amended on April 14, 2000, and (3) Claims 26 and 27 added on April 14, 2000. No new matter has been added.

Applicants summarize herein their arguments presented at the interview of August 14, 2002, which are discussed more fully below:

- Claims 2, 17, 26 and 35 of the '323 patent state that "said stochastically generated polynucleotide sequences further comprises **all twenty amino acid residues encoded at each codon position**". The only way for these polynucleotide sequences to encode every amino acid at every codon position is for the sequences to be randomly generated;
- portions of the '323 specification hint that "stochastic" might have been intended to describe completely new nucleic acids or peptides in which each position in each molecule is determined by chance during the synthesis process;
- numerous statements made by Kauffman during the prosecution of the '323 and related patents clearly state that stochastic encompasses random;
- dictionary definitions are consistent with stochastic meaning random.

Examiner Brusca has taken a very limiting interpretation of the definition of "stochastic" in Kauffman's claims. In particular, in the Office Action dated March 12, 2001 (Paper No. 29), Examiner Brusca stated the following:

The Applicants state that the Kauffman applications claim interfering subject matter. However it is the Examiner's position that the Kauffman applications do not disclose fully random peptide sequences, because the term stochastic used and claimed by Kauffman was never defined in the Kauffman applications as meaning random, and the examples of stochastic sequences disclosed in the Kauffman applications do not result in fully random sequences. Rather, the examples in the Kauffman U.S. Patent No. 5,723,3232 [sic, 5,723,323] result in sequences that are not fully random (see attached notes outlining the exemplified methods of Kauffman).

These notes simply show that one of Kauffman's prophetic examples results in two random regions flanking a constant region. The notes do not provide any basis to assume that this

prophetic example is representative of the full scope of the subject matter that Kauffman intended to claim.

Thus, the Examiner is relying on an interpretation based on what is essentially an artifact of the procedure that is used in one of the Kauffman Examples to insert the random sequences into a circularized vector. This would be clear to one of ordinary skill in the art reviewing the Kauffman specification. Moreover, the second method for making stochastic polynucleotides discussed at some length in the specification, namely the condensation of oligonucleotides, does not result in a central constant region as in the TdT method.

It is clear from reading the Kauffman patents that the main objective is to create very large libraries of nucleic acid sequences generated without regard to any known sequences. The most straightforward way to do this is to generate random nucleic acid sequences which is essentially what is described in the prophetic example relied upon by the Examiner for his interpretation. The synthesis of the polyA-polyT sequences at the end of the random sequences in this example are for the purpose of inserting the random sequences into a circularized double-stranded vector and serve no other purpose. The Examiner, however, has seized upon the inclusion of polyA-polyT sequences in the vector to support an interpretation of stochastic that incredibly excludes random sequences. Furthermore, as is explained below, this interpretation is at odds with the standard principles of claim interpretation and multiple express statements by the applicants in the file history.

While Applicants disagreed with the Examiner's interpretation of the term "stochastic" in their Response, Applicants nonetheless attempted to present claim language which fit the

Examiner's strained definition of "stochastic", in an effort to expedite the declaration of an interference. (Responses dated June 29, 2001 and August 9, 2001)

The Office Action dated July 26, 2002 maintained that Applicants did not have support in their earlier-filed application for the claim language added on August 9, 2001, for the sole purpose of accommodating Examiner Brusca's misguided interpretation of "stochastic".

Thus, Applicants have returned to their previous claims for the purposes of the declaration of an interference, and maintain that Examiner's Brusca's interpretation of "stochastic" is incorrect.

This is supported by several compelling lines of evidence including:

**The claims of the '323 patent**

The first-issued Kauffman patent, U.S. Patent No. 5,723,323 ("the '323 patent"), uses the phrase "stochastically generated polynucleotide sequences" in its independent claims. Analyzing the dependent claims leads to the inescapable conclusion that "stochastic" must at least encompass random. For example, Claims 2, 17, 26 and 35 of the '323 patent state that "said stochastically generated polynucleotide sequences further comprises all twenty amino acid residues encoded at each codon position". The only way for these polynucleotide sequences to encode every amino acid at every codon position is for the sequences to be randomly generated. Thus, the term "stochastic" in the independent claims must likewise at least encompass sequences so random that they encode all twenty amino acids at each codon position. Otherwise, they would be improper dependent claims because they would not be limiting the claims from which they depend. Indeed, the prophetic example of Kauffman upon which the Examiner relies, and which results in the stretches of As and Ts, could not encode every amino acid at every

position. Thus, the meaning of "stochastic" in the independent claims must at least encompass random sequences.

### **The '323 specification**

While the '323 specification does not provide an explicit definition of "stochastic", several portions of the '323 specification indicate that "stochastic" was intended to describe completely new nucleic acids or peptides in which each position in each molecule is determined by chance during the synthesis process. This interpretation is supported by the following statement in the specification:

The invention aims in particular at the production of stochastic genes or fragments of stochastic genes in a fashion to permit obtaining simultaneously, after transcription and translation of these genes, a very large number (on the order of at least 10,000) of **completely new proteins...**

'323 patent at Col. 1, ll. 26-31 (emphasis added).

### **File wrapper of the '323 patent**

In an Office Action dated August 12, 1991, the Examiner specifically asked the Kauffman applicants to explain what they meant by "stochastic" and related terms. The applicants declined to provide an explicit definition, and responded as follows:

Stochastic is a term of art, understandable to persons skilled in the art, especially in view of the specification.

Response filed February 12, 1992, at p. 12.

The fact that Kauffman declined to give "stochastic" a definite meaning suggests that they intended as broad a meaning as the term would allow.

In a later Response, Kauffman made another attempt to explain the meaning of the term "stochastic":

**For example, included within the definition of the term 'stochastic' is random.** As is known to those skilled in the art, this term means that claimed populations are diverse. Diversity is an inherent outcome of the **random polymerization** of, for example, nucleotide or oligonucleotide building blocks as compared to the polymerization of a defined or specific sequence.

Response dated August 23, 1995 at pp. 18-19 [Emphasis added].

Similarly, in the Response filed June 10, 1996 in Kauffman U.S. Patent No. 5,824,514, Kauffman stated in responding to a prior art rejection:

[S]uch methods do not result in or suggest the production of **random, stochastic** sequences as claimed in this invention. General knowledge at the time of the invention did not teach or suggest the production of such **random, stochastic** sequences.

Page 13 [Emphasis added].

Further evidence that the term "stochastic" is not limited to a sequence having random regions flanking a constant region as contended by the Examiner is provided by discussion in the file history relating to "partially stochastic sequences."

Included in the definition of the term stochastic is random. As is known to those skilled in the art, this term means that the claimed populations are random and as such are diverse. Diversity is an inherent outcome of the random polymerization of, for example, nucleotide or oligonucleotide building blocks as compared to the polymerization of a defined or specific sequence.

In light of the teachings within the application, the phrase "at least partially stochastic polynucleotide sequences" is intended to include sequences which are random, as described above. In addition, the phrase can include a sequence, part of which is stochastically generated, and part of which is not stochastically generated. The part that is not stochastically generated can be a known or unknown sequence. The phrase can additionally include a sequence

that contains a biased amount of any one or all of the four nucleotide triphosphate or other building blocks which comprise the polynucleotide sequence.

Response of February 5, 1998 at pp. 17-18 of '483 patent.

This discussion re-emphasizes that the defining characteristic of "stochastic" sequences is randomness, and that the presence of nonrandom as well as random sequences is not an essential feature of stochastic sequences. According to this discussion the term "partially stochastic" is used to describe a sequence having both random and nonrandom regions. If, as the Examiner contends, a stochastic sequence must have random and nonrandom regions, it would be redundant to refer to sequences having random and nonrandom regions as only "partially stochastic."

**Dictionary definition of "stochastic"**

A number of dictionary definitions are consistent with Applicants' position. For example, the American Heritage Dictionary (Houghton ed., 1976) defines "stochastic" as:

Of, denoting, or characterized by conjecture, conjectural; random or statistical.

This definition would have led the artisan to understand, before reading the '323 and other Kauffman patents, that the term "stochastic" is an adjective encompassing randomness.

**Cancellation of claims 3, 4, 6-8 and 11-27 and their reinstatement as Claims 29-48 does not violate 135(b)**

Where a "copied" claim is presented within one year from the issue date of a patent, subsequent cancellation of the claim either prior to or during the period does not preclude reinstatement of the claim for purposes of interference. *Cryns v. Musher*, 161 F.2d 217, 73 USPQ 290 (CCPA 1947); *Corbett v. Chisholm*, 568 F.2d 759, 196 USPQ 337 (CCPA 1977).

Therefore, Applicants respectfully request that an interference be declared employing the proposed Count set forth on attached Appendix B between claims 1-48 of the Kauffman '323 Patent, claims 1-5 of the Kauffman '192 Patent, claims 1-53 of the Kauffman '483 Patent, claims 1-46 of the Kauffman '514 Patent, Claims 1-107 of the Kauffman '476 Patent, Claims 1-34 of the Kauffman '862 patent and Claims 29-48 of the instant Horwitz application, all designated as corresponding to the Count. In addition, Applicants respectfully request that any pending Kauffman applications containing claims directed to the same patentable invention as defined in the Count be included in the interference.

Respectfully submitted,

Burns, Doane, Swecker & Mathis, L.L.P.

By: Sharon E. Crane  
R. Danny Huntington  
Registration No. 27,903  
Sharon E. Crane, Ph.D.  
Registration No. 36,113

P.O. Box 1404  
Alexandria, Virginia 22313-1404  
(703) 836-6620

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